229

20. (Amended) A compound of formula (I)

$$R_4$$
 N
 R_5
 R_1
 R_3
 R_1
 R_{10}
 R_2
 R_{10}

wherein

R is a halogen atom or a C1-4 alkyl group;

R, is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively are a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy, or a halogen group;

 R_4 is hydrogen, a $(CH_2)_qR_7$ or a $(CH_2)_rCO(CH_2)_\theta R_7$ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

 R_6 is hydrogen, hydroxy, amino, methylamino, dimethylamino, a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms; R_7 is hydrogen, hydroxy or NR_8R_9 wherein R_8 and R_9 are independently hydrogen or C_{1-4} alkyl optionally substituted by hydroxy, or by amino;

R₁₀ is hydrogen, a C₁₋₄ alkyl I group or

 R_{10} together with R_2 is a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3; n is zero or an integer from 1 to 3; both p and r are independently zero or an integer from 1 to 4; q is an integer from 1 to 4; provided that , when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively are a 5 to 6 membered heterocyclic group, i) m is 1 or 2; ii) when

cortal.

m is 1, R is not fluorine and iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.

- 21. (New) A compound as claimed in claim 1 wherein n is 2 and R_3 is trifluoromethyl both at the 3 and 5 position.
- 22. (New) A compound as claimed in claim 1 wherein R is selected independently from halogen or a C_{1-4} alkyl group and m is 1 or 2.
- 23. (New) A compound as claimed in claim 1 wherein m is 2, R is selected independently from halogen or methyl group at 2 or 4 position.
- 24. (New) A compound as claimed in claim 1 wherein $R_{\scriptscriptstyle 5}$ is hydrogen or a methyl group.
- 25. (New) A compound as claimed in claim 1 wherein R_1 is hydrogen or a methyl group.
- 26. (New) A compound as claimed in claim 1 wherein R_4 is hydrogen, a $(CH_2)_rCO(CH_2)_pR_7$ or $CH_2)_qR_7$ group, wherein R_7 represents an amine, both p and r are independently zero or 1; and q is 1 or 2.
- 27. (New) A compound of formula (I) as claimed in claim 1 wherein R is selected independently from halogen or methyl, R_3 is trifluoromethyl both at the 3 and 5 position, R_1 is hydrogen or methyl, R_2 is hydrogen, methyl, 2-propenyl or a cyclopropyl group or together with R_1 is a 3,6-dihydro-2H-pyridin-1-yl, a piperidin-1-yl or a pyrrolidin-1-yl group, R_{10} represents hydrogen, a methyl or R_{10} together with R_2 is a cyclopropyl group, R_4 is hydrogen, an aminoacetyl or amino ethyl group and R_5 is hydrogen or a methyl group.

- 28. (New) A compound of formula (I) as claimed in claim 1 wherein R is selected independently from halogen or methyl and m is 2, R_3 is trifluoromethyl both at the 3 and 5 position, R_1 and R_2 are independently hydrogen or methyl, R_4 is hydrogen and R_5 is hydrogen.
- 29. (New) A compound selected from:
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro methyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-methyl-4-fluoro-phenyl)-6-methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;

- 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- 2-(S)-(4-fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
 - 4-(2-amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
 - 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- [2-(3,5-bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 - [2-(3,5-bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 - 2-(3,5-bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 - 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
 - 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
 - 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; and enantiomers, pharmaceutically acceptable salts, and solvates thereof.
 - 30. (New) 2-(S)-(4-fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
 - 31. (New) 4-(2-amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 32. (Amended) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methanesulphonate.

- 33. (New) 2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 34. (New) A pharmaceutical composition comprising a compound as claimed in claim 1 in admixture with one or more physiologically acceptable carriers or excipients.
- B11
- 35. (Amended) A method for the treatment of a condition mediated by a tachykinin, in a mammal, said method comprising administering an effective amount of a compound as claimed in claim 1.
- 36. (Amended) The method of Claim 35 wherein said tachykinin is substance P or other neurokinins.
- 37. (New) The method of Claim 35 wherein said mammal is man.
- 38. (New) A process (A) for the preparation of a compound of formula (I) as claimed in claim 1, wherein R_4 is hydrogen or a $(CH_2)_qR_7$ group, provided that when R_5 is a C_{1-4} alkyl or a COR_6 group, R_5 is not in the 3 position of the piperazine ring, which comprises reduction of a compound of formula (II), wherein $(R_4)_a$ is hydrogen or a suitable nitrogen protecting group or $(R_4)_a$ is a $(CH_2)_qR_7$ group or protecting derivatives thereof; or

$$(R_4)a$$
 N
 R_5
 R_1
 R_{10}
 R_2
 R_{10}
 R_1
 R_{10}
 R_2
 R_3

PI3806USw

a process (B) for the preparation of a compound of formula (I) as claimed in claim 1, wherein R_4 is hydrogen or a $(CH_2)_rCO(CH_2)_pR_7$ group which comprises the reaction of a compound of formula (VIII), wherein $(R_4)_b$ represents a nitrogen protecting group or $(R_4)_b$ is $(CH_2)_rCO(CH_2)_pR_7$ or a protecting group thereof with triphosgene and an organic base followed by addition of the amine (V)

$$(R_4)b \longrightarrow N$$

$$NH$$

$$(R)m$$

$$(R)m$$

$$(V)$$

$$(V)$$

followed where necessary or desired by one or more of the following steps:

- (i) removal of any protecting group;
- (ii) isolation of the compound as salt thereof;
- (iii) separation of a compound of formula (I) or derivative thereof into the enantiomers thereof.

39. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound of

formula (I):

 R_4 N R_5 R_1 R_{10} R_{2} R_{3} R_{10} R_{2} R_{10}

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

PI3806USw

contol.

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)qR₇ or a (CH₂)rCO(CH₂)pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

 R_6 is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms; R_7 is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C_{1-4} alkyl optionally substituted by hydroxy or by amino; R_{10} is hydrogen, a C1-4 alkyl group or R_{10} together with R_2 represents a C_{3-7}

 κ_{10} is hydrogen, a C1-4 aikyi group or κ_{10} together with κ_2 represents a C3-7 cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 40. (New) The method according to claim 39, wherein said mammal is man.
- 41. (New) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression, unipolar depression, single

্ত

B12

major depressive episodes, recurrent major depressive episodes, dysthymic disorder, neurotic depression, social phobia, dementia of Alzheimer's type, vascular dementia with depressed mood, mood disorders induced by alcohol, mood disorders induced by amphetamines, mood disorders induced by cocaine, mood disorders induced by hallucinogens, mood disorders induced by inhalants, mood disorders induced by opioids, mood disorders induced by phencyclidine, mood disorders induced by sedatives, mood disorders induced by hypnotics, mood disorders induced by anxiolytics and schizoaffective disorder of the depressed type.

- 42. (New) The method according to claim 39, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 43. (New) The method according to claim 39, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 44. (New) The method according to claim 43, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 45. (New) The method according to claim 39, further comprising administering an effective amount of a dopaminergic antidepressant.
- 46. (New) The method according to claim 45, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 47. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

contd B12

- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;



- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;

contd.

- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 48. (New) The method according to claim 47, wherein said mammal is man.
- 49. (New) The method according to claim 47, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 50. (New) The method according to claim 47, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 51. (New) The method according to claim 50, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 52. (New) The method according to claim 47, further comprising administering an effective amount of a dopaminergic antidepressant.
- 53. (New) The method according to claim 52, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.

contd.

- 54. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 55. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 56. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 57. (New) The method according to claim 56, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 58. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 59. (New) The method according to claim 58, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 60. (New) A method for the treatment of a depressive state in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.

contd.
B12

- 61. (New) The method according to claim 60, wherein said depressive state is selected from the group consisting of bipolar depression and unipolar depression.
- 62. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound of formula (I):

$$R_4$$
 N
 R_5
 R_1
 R_3
 R_1
 R_{10}
 R_2
 R_1
 R_1
 R_2
 R_3

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)qR₇ or a (CH₂)rCO(CH₂)pR₇ group;

 R_5 is hydrogen, a C_{1-4} alkyl or a COR_6 group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms; R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino;

 R_{10} is hydrogen, a C1-4 alkyl group or R_{10} together with R_2 represents a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

eontd.

both p and r are independently zero or an integer from 1 to 4; q is an integer from 1 to 4; provided that, when R₁ and R₂ together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group, i) m is 1 or 2;

- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 63. (New) The method according to claim 62, wherein said mammal is a human.
- 64. (New) The method according to claim 62, further comprising administering an effective amount of a serotonin reuptake inhibitor.
- 65. (New) The method according to claim 64, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 66. (New) The method according to claim 62, further comprising administering an effective amount of a dopaminergic antidepressant.
- 67. (New) The method according to claim 66, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 68. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

contd. B¹²

- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;

I

- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- M
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

- 212 [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2methyl-phenyl)-piperazin-1-yl]-methanone;
 - 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)piperazin-1-yl]-methanone;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bistrifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethylphenyl)-cyclopropyl-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
 - (New) The method according to claim 68, wherein said mammal is a human. 69.
 - (New) The method according to claim 68, further comprising administering an 70. effective amount of a serotonin reuptake inhibitor.
 - (New) The method according to claim 70, wherein said serotonin reuptake 71. inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
 - (New) The method according to claim 68, further comprising administering an 72. effective amount of a dopaminergic antidepressant.
 - (New) The method according to claim 72, wherein said dopaminergic 73. antidepressant is selected from the group consisting of buproprion and amineptine.
 - (New) A method for the treatment of anxiety in a mammal comprising 74. administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methylphenyl)-4-(piperidine-4-carbonyl)-piperazine-1carboxylic acid (3,5-bistrifluoromethyl-benzyl)-methyl-amide hydrochloride.

contd B12

- 75. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 76. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 77. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 78. (New) A method for the treatment of anxiety in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 79. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I): R_5

$$R_4$$
 N R_5 R_1 R_{10} R_2 R_{10} R_2 R_{10}

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

contol.

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy or a halogen group;

 R_4 is hydrogen, a (CH₂)qR₇ or a (CH₂)rCO(CH₂)pR₇ group;

 R_5 is hydrogen, a C_{1-4} alkyl or a COR_6 group;

R₆ is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms; R₇ is hydrogen, hydroxy or NR₈R₉ wherein R₈ and R₉ represent independently hydrogen or C₁₋₄ alkyl optionally substituted by hydroxy or by amino; R₁₀ is hydrogen, a C1-4 alkyl group or R₁₀ together with R₂ represents a C₃₋₇ cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine, or a pharmaceutically acceptable salt or solvate thereof.
- 80. (New) The method according to claim 79, wherein said mammal is a human.
- 81. (New) The method according to claim 79, further comprising administering an effective amount of a serotonin reuptake inhibitor.

contd B12

- 82. (New) The method according to claim 81, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluvoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 83. (New) The method according to claim 79, further comprising administering an effective amount of a dopaminergic antidepressant.
- 84. (New) The method according to claim 83, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 85. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-biş-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)- methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;

contd. 18¹²

- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide ;
- #
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- L
- [2-(3,5-Bis-trifluoromethyl-phenyl)-pyrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-*2H*-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 - 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
 - 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide;

or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.

- 86. (New) The method according to claim 85, wherein said mammal is a human.
- 87. (New) The method according to claim 85, further comprising administering an effective amount of a serotonin reuptake inhibitor.

B12

- 88. (New) The method according to claim 87, wherein said serotonin reuptake inhibitor is selected from the group consisting of fluoxetine, cialopram, femoxetine, fluoxamine, paroxetine, indalpine, sertraline, zimeldine.
- 89. (New) The method according to claim 85, further comprising administering an effective amount of a dopaminergic antidepressant.
- 90. (New) The method according to claim 89, wherein said dopaminergic antidepressant is selected from the group consisting of buproprion and amineptine.
- 91. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 92. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 93. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 94. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.

contd. B12

- 95. (New) A method for the treatment of a panic disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 96. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound of formula (I): R_5

$$R_4$$
 N
 R_5
 R_1
 R_3
 R_3
 R_4
 R_4
 R_5
 R_1
 R_{10}
 R_2
 R_3

wherein:

R is a halogen atom or a C₁₋₄ alkyl group;

R₁ is hydrogen or a C₁₋₄ alkyl group;

 R_2 is hydrogen, a C_{1-4} alkyl, C_{2-6} alkenyl or a C_{3-7} cycloalkyl group; or R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5-6 membered heterocyclic group;

 R_3 is a trifluoromethyl, a C_{1-4} alkyl, a C_{1-4} alkoxy, a trifluoromethoxy or a halogen group;

R₄ is hydrogen, a (CH₂)qR₇ or a (CH₂)rCO(CH₂)pR₇ group;

R₅ is hydrogen, a C₁₋₄ alkyl or a COR₆ group;

 R_6 is hydrogen, hydroxy, amino, methylamino, dimethylamino a 5 membered heteroaryl group containing 1 to 3 heteroatoms selected from oxygen, sulphur and nitrogen or a 6 membered heteroaryl group containing 1 to 3 nitrogen atoms; R_7 is hydrogen, hydroxy or NR_8R_9 wherein R_8 and R_9 represent independently hydrogen or C_{1-4} alkyl optionally substituted by hydroxy or by amino;

PI3806USw

B12

 R_{10} is hydrogen, a C1-4 alkyl group or R_{10} together with R_2 represents a C_{3-7} cycloalkyl group;

m is zero or an integer from 1 to 3;

n is zero or an integer from 1 to 3;

both p and r are independently zero or an integer from 1 to 4;

q is an integer from 1 to 4;

provided that, when R_1 and R_2 together with nitrogen and carbon atom to which they are attached respectively represent a 5 to 6 membered heterocyclic group,

- i) m is 1 or 2;
- ii) when m is 1, R is not fluorine and
- iii) when m is 2, the two substituents R are not both fluorine,

or a pharmaceutically acceptable salt or solvate thereof.

- 97. (New) The method according to claim 96, wherein said mammal is a human.
- 98. (New) The method according to claim 96, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 99. (New) The method according to claim 96, further comprising administering an effective amount of a 5HT3 antagonist.
- 100. (New) The method according to claim 99, wherein said 5HT3 antagonist is selected from the group consisting of ondansetron, granisetron and metoclopramide.
- 101. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of a compound selected from the group consisting of
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Isopropyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;

B12

- 2-(4-Fluoro-3-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-Difluoro-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(4-Fluoro-phenyl)- piperazine-1-carboxylic acid (3,4-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-Phenyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(3,4-dichloro-phenyl)-piperazine-1-carboxylic acid (3,5-bistrifluoro-methyl-benzyl)-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-3-methyl-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(2-Methyl-4-Fluoro-phenyl)-6-Methyl- piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)ethyl]-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 4-(2-Amino-ethyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide;
- 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(1-3,5-bis-trifluoromethyl-phenyl)-cyclopropyl]-methyl-amide;
- [2-(3,5-Bis-trifluoromethyl-phenyl)-p'yrrolidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;

eontol.

- [2-(3,5-Bis-trifluoromethyl-phenyl)-3,6-dihydro-2H-pyridyn-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(3,5-Bis-trifluoromethyl-phenyl)-piperidin-1-yl]-[2-(S)-(4-fluoro-2-methyl-phenyl)-piperazin-1-yl]-methanone;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-but-3-enyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(3,5-bis-trifluoromethyl-phenyl)-2-methyl-propyl]-methyl-amide;
- 2-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [(3,5-bis-trifluoromethyl-phenyl)-cyclopropyl-methyl]-methyl-amide; or an enantiomer, or pharmaceutically acceptable salt or solvate thereof.
- 102. (New) The method according to claim 101, wherein said mammal is a human.
- 103. (New) The method according to claim 101, wherein said gastrointestinal _ disorder is irritable bowel syndrome.
- 104. (New) The method according to claim 101, further comprising administering an effective amount of a 5HT3 antagonist.
- 105. (New) The method according to claim 104, wherein said 5HT3 antagonist is selected from ondansetron, granisetron and metoclopramide.
- 106. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-4-(piperidine-4-carbonyl)-piperazine-1carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.
- 107. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 4-(2-Amino-acetyl)-2-(S)-(4-fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid (3,5-bis-trifluoromethyl-benzyl)-methyl-amide hydrochloride.

contal.

- 108. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.
- 109. (New) The method according to claim 108, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 110. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide methansulphonate.
- 111. (New) The method according to claim 110, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 112. (New) A method for the treatment of a gastrointestinal disorder in a mammal comprising administering to said mammal an effective amount of 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide acetate.
- 113. (New) The method according to claim 112, wherein said gastrointestinal disorder is irritable bowel syndrome.
- 114. (New) 2-(S)-(4-Fluoro-2-methyl-phenyl)-piperazine-1-carboxylic acid [1-(R)-(3,5-bis-trifluoromethyl-phenyl)-ethyl]-methyl-amide or an enantiomer or pharmaceutically acceptable salt or solvate thereof.